

Claims

1. An isolated nucleic acid molecule selected from the group consisting of:
- 5 (a) a nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:1; and
- (b) a nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:3.
- 10 2. An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2.
3. An isolated nucleic acid molecule comprising the nucleotide sequence contained in the plasmid deposited with ATCC® as Accession Number _____.
- 15 4. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2.
- SAB*
A 9
20 5. An isolated nucleic acid molecule selected from the group consisting of:
- (a) a nucleic acid molecule comprising a nucleotide sequence which is at least 50% homologous to the nucleotide sequence of SEQ ID NO:1 or 3, or a complement thereof;
- (b) a nucleic acid molecule comprising a fragment of at least 250 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or 3, or a complement thereof;
- 25 (c) a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence at least about 45% homologous to the amino acid sequence of SEQ ID NO:2; and
- (d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 15 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2.

6. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5 under stringent conditions.

5 7. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the nucleotide sequence of the nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5.

10 8. An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5, and a nucleotide sequence encoding a heterologous polypeptide.

5 9. A vector comprising the nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5.

15 10. The vector of claim 9, which is an expression vector.

11. A host cell transfected with the expression vector of claim 10.

20 12. A method of producing a polypeptide comprising culturing the host cell of claim 11 in an appropriate culture medium to, thereby, produce the polypeptide.

13. An isolated polypeptide selected from the group consisting of:

25 (a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2;

30 (b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule consisting of SEQ ID NO:1 or 3 under stringent conditions;

(c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 50 % homologous to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or 3;

5 (d) a polypeptide comprising an amino acid sequence which is at least 45% homologous to the amino acid sequence of SEQ ID NO:2.

14. The isolated polypeptide of claim 13 comprising the amino acid sequence of SEQ ID NO:2.

10 15. The polypeptide of claim 13, further comprising heterologous amino acid sequences.

16. An antibody which selectively binds to a polypeptide of claim 13.

15 17. A method for detecting the presence of a polypeptide of claim 13 in a sample comprising:

(a) contacting the sample with a compound which selectively binds to the polypeptide; and

20 (b) determining whether the compound binds to the polypeptide in the sample to thereby detect the presence of a polypeptide of claim 13 in the sample.

18. The method of claim 17, wherein the compound which binds to the polypeptide is an antibody.

25 19. A kit comprising a compound which selectively binds to a polypeptide of claim 13 and instructions for use.

20. A method for detecting the presence of a nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5 in a sample comprising:

30 (a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule; and

SEARCHED
INDEXED
MAILED
FILED
JULY 1998
U.S. PATENT AND TRADEMARK OFFICE

(b) determining whether the nucleic acid probe or primer binds to a nucleic acid molecule in the sample to thereby detect the presence of a nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5 in the sample.

5 21. The method of claim 20, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

22. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5 and instructions for use.

10 23. A method for identifying a compound which binds to a polypeptide of claim 13 comprising:

(a) contacting the polypeptide, or a cell expressing the polypeptide with a test compound; and

15 (b) determining whether the polypeptide binds to the test compound.

24. A method for identifying a compound which modulates the activity of a polypeptide of claim 13 comprising:

(a) contacting a polypeptide of claim 13 with a test compound; and

20 (b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

25 25. A method for modulating the activity of a polypeptide of claim 13 comprising contacting the polypeptide or a cell expressing the polypeptide with a compound in a sufficient concentration to modulate the activity of the polypeptide.

26. A transgenic animal generated from a cell genetically engineered to lack nucleic acid encoding a AS3 polypeptide, said transgenic animal lacking expression of said AS3 polypeptide.

30

27. A transgenic animal generated from a cell that contains a substantially pure nucleic acid replacing DNA encoding a AS3 polypeptide, wherein said nucleic acid is expressed in said transgenic animal.

5 28. A method of identifying a compound that modulates cell proliferation, said method comprising:

- (a) providing a cell comprising a *AS3* gene; and
- (b) contacting said cell with a candidate compound; and
- (c) monitoring expression of said *AS3* gene, wherein an alteration in the level of expression of said gene indicates a compound which modulates cell proliferation.

10 29. A method of identifying a compound that modulates cell proliferation, said method comprising:

- (a) providing a cell comprising a reporter gene operably linked to a promoter from a *AS3* gene;
- (b) contacting said cell with a candidate compound; and
- (c) measuring expression of said reporter gene, an alteration in said expression in response to said candidate compound identifying a compound that is able to modulate cell proliferation.

20 30. The method of claim 28 or 29, wherein said alteration is an increase indicating said compound is an inhibitor of cell proliferation.

25 31. A method of inhibiting the proliferation of a cell, said method comprising administering to said cell an amount of AS3 polypeptide or fragment thereof sufficient to inhibit cell proliferation.

30 32. A method of inhibiting cell proliferation in a mammal, said method comprising providing a transgene encoding a AS3 polypeptide or fragment thereof to a cell of said mammal, said transgene being positioned for expression in said cell.

33. A method of inhibiting cell proliferation in a cell, said method comprising administering a compound which increases AS3 activity.

34. The method of claim 31, 32, or 33, wherein said AS3 is from a mammal.

5

35. The method of claim 31, 32, or 33, wherein said cell is in a mammal.

36. The method of claim 31, 32, or 33, wherein said cell is in a mammal diagnosed as having a condition involving cell proliferation.

10

37. The method of claim 36, wherein said condition is cancer.

38. The method of claim 37, wherein said cancer is prostate cancer.

15

39. A method of diagnosing a mammal for the presence of disease involving altered cell proliferation or an increased likelihood of developing a disease involving altered cell proliferation, said method comprising isolating a sample of nucleic acid from said mammal and determining whether said nucleic acid comprises a AS3 mutation, said mutation being an indication that said mammal has a cell proliferative disease or an increased likelihood of 20 developing a disease involving cell proliferation.

20

40. A method of diagnosing a mammal for the presence of a disease involving altered cell proliferation or an increased likelihood of developing a disease involving altered cell proliferation, said method comprising measuring AS3 gene expression in a sample from said mammal, an alteration in said expression relative to a sample from an unaffected mammal being an indication that said mammal has a cell proliferative disease or increased likelihood of developing an cell proliferative disease.

25

41. The method of claim 40, wherein said gene expression is measured by assaying 30 the amount of AS3 polypeptide or AS3 biological activity in said sample.

DO NOT RESEND OR RECOPY THIS DOCUMENT

42. The method of claim 41 wherein said AS3 polypeptide is measured by immunological methods or by assaying the amount of AS3 RNA in said sample.

43. The method of claim 40 or 41, wherein said mammal is a human.

5

44. The method of claim 40, wherein said measuring is performed after or concurrent with the administration of a hormone to said mammal.

10

45. The method of claim 44, wherein said hormone as an androgen.

46. A kit for diagnosing a mammal for the presence of a disease involving altered cell proliferation or an increased likelihood of developing a disease involving altered cell proliferation, said kit comprising a substantially pure antibody that specifically binds a AS3 polypeptide.

20

15
A10
47. A kit for diagnosing a mammal for the presence of a disease involving altered cell proliferation or an increased likelihood of developing a disease involving altered cell proliferation, said kit comprising a material for measuring AS3 RNA.

25

48. A method of obtaining a AS3 polypeptide, said method comprising:
(a) providing a cell with DNA encoding a AS3 polypeptide, said DNA being positioned for expression in said cell;

(b) culturing said cell under conditions for expressing said DNA; and

(c) isolating said AS3 polypeptide.

30

49. A method of isolating a AS3 gene or portion thereof having sequence identity to human AS3, said method comprising amplifying by polymerase chain reaction said AS3 gene or portion thereof using oligonucleotide primers wherein said primers

(a) are each greater than 15 nucleotides in length;

(b) each have regions of complementarity to opposite DNA strands in a region of the nucleotide sequence of SEQ ID NO: 1; and

(c) optionally contain sequences capable of producing restriction endonuclease cut sites in the amplified product; and isolating said AS3 gene or portion thereof.

50. A method of detecting if a subject is at increased risk of developing prostate
5 cancer comprising directly or indirectly:

- (a) detecting levels of AS3 nucleic acid or polypeptide; and
(b) observing if the subject has AS3 levels that are reduced as compared to a standard wherein said reduced AS3 levels indicate said subject is at increased risk of developing prostate cancer.

10 51. A kit for determining if a subject is at increased risk of developing prostate
cancer comprising:

- (a) at least one reagent that specifically detects an AS3 molecule, wherein said reagent is selected from the group consisting of antibodies that selectively bind AS3, and
15 oligonucleotide probes that selectively bind to DNA encoding AS3; and
(b) instructions for determining that the subject is at increased risk of developing prostate cancer by
(c) detecting the presence or absence of AS3 in said subject with at least one reagent; and
20 (d) observing whether or not the subject is at increased risk of developing prostate cancer by observing if the presence of AS3 is or is not detected with said at least one reagent, wherein reduced or absent levels of AS3 indicates said subject is at increased risk of developing prostate cancer.

25 52. A method of prognosis for prostate cancer comprising:

- (a) obtaining a biological sample from a subject;
(b) measuring AS3 nucleic acid or polypeptide levels in said sample;
(c) correlating said AS3 level with a baseline level, wherein the baseline level is determined by measuring levels of AS3 in disease free subjects;
30 (d) correlating levels of AS3 at baseline or below, which is a negative result, with a poorer prognosis than a positive result, wherein the level of AS3 is above the baseline level.

53. The method of claim 52, wherein said measuring is performed after or concurrent with the administration of a hormone to said mammal.

54. The method of claim 52, wherein said hormone as an androgen.

55. The method of claim 52, wherein the level of AS3 is measured with an antibody or antibody fragment thereof that selectively binds AS3.

56. The method of claim 52, wherein the level of AS3 is measured with an nucleic acid probe or primer that selectively binds AS3.

57. A method of treating prostate cancer comprising,
(a) identifying a subject having or about to have prostate cancer;
(b) administering a hormone to said subject; and
15 (c) determining if said subject exhibits an increase in AS3 levels.

58. The method of claim 57, wherein the method further includes determining that said subject exhibiting an increase in AS3 levels is likely to be responsive to the inhibitory effect of androgens as compared to a subject not exhibiting an increase in AS3
20 levels.

59. The method of claim 57, wherein said subject showing an increase in AS3 levels is a candidate for hormone treatment.

25 60. The method of claim 59, wherein said subject showing an increase in AS3 levels is indicated as being a candidate for intermittent hormone treatment.

61. The method of claim 57, wherein the hormone is an androgen.

30 62. The method of claim 57, wherein the subject is a human.

63. The method of claim 57, wherein said AS3 levels are nucleic acid

levels or polypeptide levels.

64. The method of claim 57, wherein the level of AS3 is measured with an antibody or antibody fragment thereof that selectively binds AS3.

5

65. The method of claim 57, wherein the level of AS3 is measured with an nucleic acid probe or primer that selectively binds AS3.

66. A method of diagnosing a mammal for the presence of disease associated with
10 AS3 or an AS3 related molecule or an increased likelihood of developing a disease
associated with an AS3 or an AS3 related molecule, said method comprising isolating a
sample of nucleic acid from said mammal and determining whether said nucleic acid
comprises a mutation in an AS3 or AS3 related molecule, said mutation being an indication
that said mammal has a disease associated with AS3 or an AS3 related molecule or an
15 increased likelihood of developing a disease associated with an AS3 or an AS3 related
molecule.

67. A method of diagnosing a mammal for the presence of a disease associated with
AS3 or an AS3 related molecule or an increased likelihood of developing a disease
20 associated with an AS3 or an AS3 related molecule, said method comprising measuring
expression levels of AS3 or an AS3 related molecule in a sample from said mammal, an
alteration in said expression relative to a sample from an unaffected mammal being an
indication that said mammal has a disease or increased likelihood of a disease associated
with AS3 or an AS3 related molecule.

25